EXHIBIT 24

1: Rapid Commun Mass Spectrom. 2005;19(15):2123-30.

Comparison of negative and positive ion electrospray ionization mass spectra of calmodulin and its complex with trifluoperazine.

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The protein calmodulin (apoCaM) undergoes a conformational change when it binds calcium. This structure of the protein (Ca4CaM) is a dumbbell-shaped molecule that undergoes a further profound conformational change on binding of the antipsychotic drug trifluoperazine (TFP). Experimental conditions were developed to prepare samples of apoCaM, Ca4CaM and Ca4CaM/TFP that were substantially free of sodium. The effects of the conformational changes of calmodulin on the charge-state distributions observed in positive ion and negative ion electrospray ionization (ESI) mass spectra were examined. Conversion of apoCaM into Ca4CaM was concomitant with a change in the negative ion ESI mass spectrum whereby the 16- ion was the most abundant ion observed for the apo form and the 8- ion was the most abundant for the complex. In contrast, in the positive ion ESI mass spectra of apoCaM and Ca4CaM, the most abundant species in each case was the 8+ ion. When a complex of Ca4CaMwith TFP was prepared, the most abundant species was the 5+ ion. This is consistent with a conformational change of Ca4CaM that rendered some basic sites inaccessible to ionization in the ESI process. Using the same Ca4CaM/TFP mixture, no complex with TFP was observed in negative ion ESI mass spectra. These observations are discussed in the context of the structural changes that are known to occur in calmodulin, and suggestions are made to explain the apparently conflicting data. The results reported here reflect on the validity of using differences in charge-state distributions observed in ESI mass spectra to assess conformational changes in proteins. (c) 2005 John Wiley & Sons, Ltd.

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